REMARKS

The Office Action mailed 3 January 2011, has been received and its contents carefully noted. Claims 1-2, 4-5, 7-10, 12-14, 18, 21, 26-28, 30-34, 38 and 46-58 were pending and claims 1-2, 4-5, 7-10, 12-14, 18, 21, 26-28, 30-32 and 46-58 were rejected. By this amendment, claims 1, 4-5, 8, 10, 18, 21, 26-28, 30-31, 46, 48-52, 54 and 56-58 have been amended and claims 2, 12-14, 33-34 and 38 have been canceled. Support may be found in the specification and the claims as originally filed. No statutory new matter has been added. Therefore, reconsideration and entry of the claims as amended are respectfully requested.

Objection to the Specification

The Examiner objected to the specification for improper use of trademarks.

Applicants respectfully requests that this rejection be held in abeyance until an indication of allowable subject matter.

Claim Objections

The Examiner objected to claims 1-2, 4, 5, 46 and 57 for various informalities.

Applicants respectfully submit that the claim objections may be withdrawn in view of the amendments made thereto.

Rejections under 35 U.S.C. 112, second paragraph

The Examiner rejected claims 8, 13, 18, 21, 26-28, 30, 31, 46, 48, 49, 50, 52, 54, 56, and 58 under 35 U.S.C. 112, second paragraph, as being indefinite.

Applicants respectfully submit that the claims, as amended, are clear and definite. Therefore, the rejections under 35 U.S.C. 112, second paragraph, should properly be withdrawn.

Rejections under 35 U.S.C. 112, first paragraph

The Examiner rejected claims 1, 2, 4, 5, 12-14, 18, 21, 26, 28, 30-32, and 46-58 under 35 U.S.C. 112, first paragraph, as failing to comply with the written requirement. The Examiner rejected claims 1, 2, 4, 5, 7-10, 12-14, 18, 21, 26, 28, 30-32, and 46-58 as failing to comply with the enablement requirement. Nevertheless, the Examiner conjugates comprising trastuzumab,

triaminobenzene, tricarboxybenzene, diacarboxyaniline, or diamino benzoic acid as the trifunctional linking moiety, and biotin or a biotin derivative as set forth in claim 13 and compositions and kits comprising such have adequate written description and enabling support.

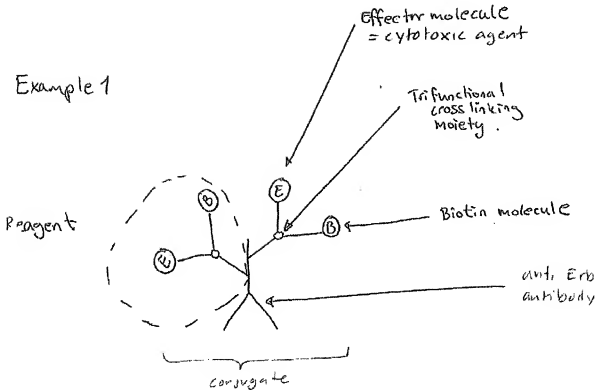
Applicants respectfully submit that the claims, as amended, have adequate written description and enabling support. Specifically, the claims have been amended such that the antibody is trastuzumab, the trifunctional linking moiety is triaminobenzene, tricarboxybenzene, diacarboxyaniline, or diamino benzoic acid, and the affinity ligand is biotin, or a biotin derivative selected from the group consisting of norbiotin, homobiotin, oxybiotin, iminobiotin, destibiotin, diaminobiotin, biotin sulfoxide, biotin sulfone, and derivatives thereof having an affinity-binding constant of at least $10^9 M^{-1}$.

Therefore, Applicants respectfully submit that the rejections under 35 U.S.C. 112, first paragraph, should properly be withdrawn.

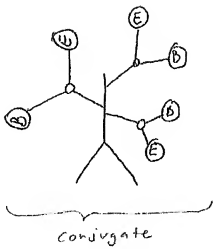
Rejections under 35 U.S.C. 103(a)

The Examiner rejected claims 1, 2, 5, 12-13, 18, 21, 28, 46-50, 57, and 58 under 35 U.S.C. 103(a) as being unpatentable over WO 97/29114 in view of WO 99/55367 or WO 01/00244. The Examiner rejected claims 1, 2, 5, 7-10, 12-14, 18, 21, 26, 28, 30, 31, and 46-58 as being unpatentable over WO 00/02050 in view of WO 99/55367 or WO 01/00244. The Examiner also rejected claims 1, 2, 4, 5, 7-10, 12-14, 18, 21, 26-28, 30, 31, and 46-58 as being unpatentable over WO 00/02051 in view of WO 99/55367 or WO 01/00244. Each of these rejections is traversed.

Applicants respectfully submit that the conjugate according to the present invention contained an average of 2-4 molecules of a) a tri-functional cross-linking moiety, b) an affinity ligand, and c) a cytotoxic agent, bound to one anti Erb antibody (trastuzumab). The conjugate according to the present invention advantageously allows one to increase the dose or amount of a cytotoxic agent that is administered to a subject as compared to current established therapeutic amounts for cancer treatments. With a view to illustrating the overall structure of the inventive conjugate in a different way, Applicants respectfully submit the following drawing:



Example 2



As set forth in the drawing, E means the cytotoxic agent (effector molecule), B means biotin (affinity ligand) and the reagent means the structural features a)-c) in claim 1. In Example

1 of the drawing, the conjugate contains two cytotoxic agents, and in Example 2 of the drawing, the conjugate contains three cytotoxic agents.

Administration of a medical agent containing a cytotoxic agent bound to a tumor surface specific molecule, in this case an anti Erb antibody, i.e. trasuzumab, results in a specific binding of a certain amount of the medical agent to the tumor surface, while the remaining amount of the non-bound medical agent remains for days or weeks in the blood circulation and exposes the body for undesired cytotoxic effects on healthy tissues and organs. Thus, for each kind of cytotoxic agent, a maximum dose to be administered to a subject has been established in the medical community in order to minimize or avoid undesired cytotoxic effects. In addition, prior art cancer therapies administer only one cytotoxic agent per antibody to cancer patients.

However, according to the present invention, more than one, i.e. an average of 2-4, cytotoxic agents per antibody in the conjugate, i.e. the medical agent, may be administrated to a subject. Thus, a higher dose of the cytotoxic agent is effectively targeted close to the tumor surface, to which the antibody part of the conjugate binds and where the cytotoxic agents may exert a therapeutic benefit, e.g. anti-tumor benefit. In other words, the conjugates according to the present invention provide an increased concentration cytotoxic medical agents to tumor cells while decreasing undesired cytotoxicity.

Further, the presence of an average of 2-4 affinity ligands, e.g. biotin, in addition to an average of 2-4 cytotoxic agents in the conjugate facilitates and speeds up the extracorporeal removal of undesired remaining conjugates containing cytotoxic agents circulating in the blood of a subject. Specifically, the adsorption rate of an extracorporeal filter that is used for removing unbound conjugates circulating in the blood of a subject is increased by the increased amount of affinity ligands per conjugate. Thus, the conjugates according to the present invention reduce the time needed for removal of unbound conjugates as compared to the time needed for prior art chemotherapeutics. Consequently, the conjugates of the present invention allow the administration of a higher total dose of a cytotoxic agent to a cancer patient without increasing undesired cytotoxicity as compared to prior art therapeutics.

In addition, the conjugates of the present invention have a unique structure that makes it stable, both on its way to the tumor surface and when present in the blood circulation, which substantially reduces the risk for harmful effects on tissues and organs before the conjugates are

extracorporeally eliminated from the subject's body. Moreover, the unique structure does not negatively influence the binding properties, the biodistribution, and the biokinetics of the anti-Erb antibody.

Nowhere do the cited documents, alone or in combination, teach or suggest binding several molecules, i.e. a)-c) of claim 1, which include both a cytotoxic agent and an affinity ligand, to the one and same antibody in to form a conjugate suitable for use in treatments against cancer or the unexpected advantages of the conjugate – the ability to deliver higher concentrations of medical agents to a tumor without increasing undesired cytotoxicity, easier and faster removal of unbound conjugates circulating in the blood, and improved stability.

Therefore, Applicants respectfully submit that the claims, as amended, are unobvious and the rejections under 35 U.S.C. 103(a) should be withdrawn.

Request for Interview

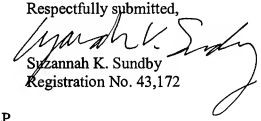
Either a telephonic or an in-person interview is respectfully requested should there be any remaining issues.

CONCLUSION

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Therefore, it is respectfully requested that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. It is believed that a full and complete response has been made to the outstanding Official action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

It is not believed that extensions of time are required, beyond those that may otherwise be provided for in accompanying documents. However, in the event that additional extensions of time are necessary to prevent abandonment of this application, then such extensions of time are hereby petitioned under 37 C.F.R. 1.136(a), and any fees required therefor are hereby authorized to be charged to **Deposit Account No. 024300, Attorney Docket No. 033972.011.**

Respectfully submitted,



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